

## REMARKS

### **Status of the Claims**

Claims 1-35 are pending in the instant application. Claims 13-27 and 29-32 are withdrawn from further consideration pursuant to the provisions of 37 CFR 1.142(b), as being drawn to nonelected inventions.

Claims 1-12, **28** (emphasis added), and 33-35 read on the elected invention and under examination. For the sake of clarity, the undersigned respectfully directs the Examiner's attention to the fact that the Office Action mistakenly indicates that claim 29 "reads on the invention" and is under examination (Office Action, page 2). Based on the claim designations used in the Disposition of Claims portion of the Office Action Summary, it is apparent that the Examiner meant to indicate that claim 28, not claim 29, reads on the elected invention.

Section 9 of the Office Action indicates that claims 28 and 33-35 recite allowable subject matter.

### **Modification of the Restriction Requirement**

The requirement for restriction which was imposed on May 3, 2006 instructed the Applicants to restrict the subject matter of the instant application to Groups 1-X', wherein X' represents the number of combinations of the amino acid sequences that result from the various combinations of V<sub>H</sub> and V<sub>L</sub> sequences recited in the original claims.

In response to the Restriction Requirement, Applicants proposed three new claims (claims 33-35) each of which define a group of anti-VEGF antibodies which share a common feature (i.e., a V<sub>H</sub> or V<sub>L</sub> sequence). A review of the claim listing submitted in response to the Restriction Requirement indicates that Applicants restructured the claim set and proposed 4 groups of anti-VEGF monoclonal antibodies, for examination in combination with the linking claims (i.e., claims 1-12) identified by the Examiner. The groups of antibodies suggested by Applicants consisted of: (claim 28 and claims 1-12); , ( claim 33 and claims 1-12), ( claim 34 and claims 1-12) and (claim 34 and claims 1-12). Each group of antibodies proposed by Applicants included antibodies that were defined by reference to specific SEQ ID NOS: for their V<sub>H</sub> and V<sub>L</sub> sequences.

In order to be fully responsive to the Restriction Requirement Applicants provisionally elected, with traversal, the subject matter of the linking claims (claims 1-12) and 35, which recites a single anti-VEGF monoclonal comprising a V<sub>L</sub> and V<sub>H</sub> pair consisting of SEQ ID NO: 28 and SEQ ID NO: 106, respectively for examination on the merits.

Applicants acknowledge the Examiner's decision to withdraw the restriction between the antibody pairs recited in claim 33 and appreciated the opportunity to have the antibodies defined by the pair wise combination of the seven V<sub>H</sub> sequences identified by specific SEQ ID NOS: (SEQ ID NOS: 88, 90, 91, 106, 107, 108 and 109) in combination with three V<sub>L</sub> sequences identified by specific SEQ ID NOS: (SEQ ID NOS: 26, 28 and 36) as a single invention.

#### **Claim Amendments**

Claims 1-6 and 10-12 have been canceled. Claims 33-35 were previously presented. Claims 36-49 are newly presented. The claim amendments and the subject matter of new claims find support in the specification as filed and do not introduce any new matter into the application.

Claims 7-9 have been amended to change their base claim from Claim 1, now canceled, to Claim 33, which the Examiner has indicated recites allowable subject matter. No new matter has been introduced by virtue of the amendments.

Claims 36-39 find support in paragraph 287 of the published application US2004/0133357. Claims 40 – 44 are generally supported in paragraphs 244-246 of the published application. Claim 40 recites the CDR sequences (i.e., CDR1, CDR2 and CDR3) for the light chain variable domain (V<sub>L</sub>) SEQ ID NO: 28. Claim 41 recites the CDR sequences for the heavy chain variable domain (V<sub>H</sub>) SEQ ID NO: 106. These claims are also supported by the data presented in Figure 2C for the anti-VEGF variant hAB35 and paragraph 51 of the published application, which indicates that hAB35 contains a V<sub>L</sub> and V<sub>H</sub> pair SEQ ID NO: 28 and SEQ ID NO: 106. One of skill in the art would have no trouble discerning the SEQ ID NOS that correspond to the CDR regions (i.e., CDR1, CDR2 and CDR3) of the heavy chain variable and light chain variable regions consisting of the amino acid sequences set forth in SEQ ID NO: 28 (V<sub>L</sub>) and SEQ ID NO: 106 (V<sub>H</sub>).

Claim 45 recites the CDR sequences for SEQ ID NO: 26 (V<sub>L</sub>). It is supported by paragraphs 242 and 244-246 of the published application.

Claim 46 recites the CDR sequences for SEQ ID NO: 106 (V<sub>H</sub>). It is supported by paragraphs 243 and 246 of the published application. It is also supported by the data presented in Figure 2C for hAB35 which comprises SEQ ID NO: 106.

Claim 47 recites the CDR sequences for SEQ ID NO: 36 (V<sub>L</sub>). It is supported by paragraphs 242 and 244-246 of the published application.

Claim 48 recites the seven heavy chain variable domains included in the pairwise combinations of V<sub>L</sub> and V<sub>H</sub> set forth in claim 33.

Claim 49 recites the three light chain variable domains included in the pairwise combinations of V<sub>L</sub> and V<sub>H</sub> set forth in claim 33.

**Amendment of the Specification**

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. As indicated above, Applicants have included an instruction to amend the paragraph cited in the Office Action, to eliminate the embedded hyperlink and/or browser-executable code which was present in the disclosure as filed.

Based on the above-described amendment, Applicants request reconsideration and withdrawal of the objections to the specification.

**Rejection of Claims 2-6 under 35 USC §112, First Paragraph**

Claims 2-6 are rejected under 35 USC §112, first paragraph, for allegedly failing to comply with the enablement requirement. The rejected claims are drawn to monoclonal antibodies that specifically bind to human VEGF with Kd equal to or lower than 0.1 nM, 0.08 nM, 0.05 nM, 0.01 nM and 0.005 nM. The Examiner states that the rejected claims contain "subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention"(Office Action, page 3).

This rejection has been obviated by Applicant's cancellation of claims 2-6. Applicants request reconsideration and withdrawal of the enablement rejection.

**Rejection of Claims 1 and 7-12 under 35 USC §102(b)**


Claims 1 and 7-12 are rejected under 35 USC §102(b) for allegedly being anticipated by Baca *et al.* (WO 98/45331).

This rejection is partially obviated by the cancellation of Claims 1 and 10-12. The rejection is also obviated with respect to Claims 7-9, in light of the amendment introduced into each of these claims which changes their base claim from claim 1 to claim 33. As amended, claims 7-9 are dependent upon a claim (i.e, Claim 33) which the Examiner has found to recite allowable subject matter.

U.S.S.N.: 10/723,434  
Case No.: AX0001ID  
Page No: 13  
Date: July 23, 2007

In light of the cancellation of claims 1 and 10-12 and the amendments made to claims 7-9,  
Applicants request reconsideration and withdrawal of the rejection under 35 USC §102(b).

Respectfully submitted,

By   
Patricia Chisholm  
Reg. No. 45,822  
Attorney

MERCK & CO., INC.  
P.O. Box 2000  
Rahway, New Jersey 07065-0907  
(732) 594-5738